

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 13 November 2000 (13.11.00)	
International application No. PCT/US00/06482	Applicant's or agent's file reference 175961
International filing date (day/month/year) 10 March 2000 (10.03.00)	Priority date (day/month/year) 12 March 1999 (12.03.99)
Applicant MARCUS, Monica, G. et al	

1. The designated Office is hereby notified of its election made:

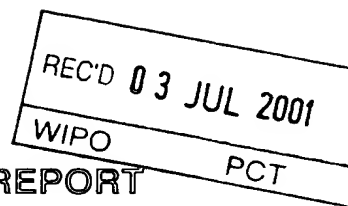
☒ in the demand filed with the International Preliminary Examining Authority on:
12 October 2000 (12.10.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Kiwa Mpay Telephone No.: (41-22) 338.83.38
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 175961	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/06482	International filing date (day/month/year) 10/03/2000	Priority date (day/month/year) 12/03/1999
International Patent Classification (IPC) or national classification and IPC A61K31/00		
Applicant THE UNITED STATES OF AMERICA, represented by THE;		



- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of 1 sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 12/10/2000	Date of completion of this report 26.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Hoff, P Telephone No. +31 70 340 3520 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/06482

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-16 as originally filed

Claims, No.:

1-13 as originally filed

14-23 as received on 07/05/2001 with letter of 03/05/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/06482

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☒ the entire international application.

☐ claims Nos. .

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-23.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/06482

Re Item I

Basis of the report

The amendments filed with the letter dated 03.05.01 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT. The amendments concerned are the following:

- the method of inhibiting cellular proliferation and cancer with coumarin or a coumarin derivative (claims 14-15)
- the method of inhibiting hepatitis B virus with coumarin or a coumarin derivative (claim 17)
- the method of modulating the effect of the steroid hormone receptor with coumarin or a coumarin derivative (claim 19)
- the method of inhibiting the response of Hsf-1 to stress with coumarin or a coumarin derivative (claim 21)

No basis for such an extension can be found in the application as filed. There is no disclosure in the application as filed of such conditions intended to be treated with coumarin or a coumarin derivative.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims relating to inventions in respect of which no international search report has been established need not to be the subject of an international preliminary examination (Rule 66.1(e) PCT). The EPO policy when acting as an International Preliminary Examining Authority is not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims have been amended during any Chapter II procedure.

13. The method of claim 12, wherein the client protein or the client polypeptide is degraded.

14. The method of any of claims 1-13, wherein the chaperone protein is in a cell and cellular proliferation is inhibited.

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15. The method of claim 14, wherein the cellular proliferation is cancer.

16. The method of any of claims 1, 3-6, 12 and 13, wherein the client protein is hepatitis B virus reverse transcriptase.

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17. The method of claim 16, whereupon hepatitis B virus is inhibited.

18. The method of any of claims 1, 3-6, 12 and 13, wherein the client protein is a steroid hormone receptor.

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19. The method of claim 18, wherein the effect of the steroid hormone receptor is modulated.

20. The method of any of claims 1, 3-6, 12 and 13, wherein the client protein is in a cell and is Hsf-1.

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21. The method of claim 20, wherein the response of Hsf-1 to stress is inhibited.

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22. The method of any of claims 1-21, which is *in vivo*.

23. The method of any of claims 1-21, which is *ex vivo*.



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 31/00	A2	(11) International Publication Number: WO 00/53169 (43) International Publication Date: 14 September 2000 (14.09.00)
(21) International Application Number: PCT/US00/06482 (22) International Filing Date: 10 March 2000 (10.03.00) (30) Priority Data: 60/124,135 12 March 1999 (12.03.99) US (71) Applicant (for all designated States except US): THE UNITED STATES OF AMERICA, represented by THE SECRETARY DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): MARCU, Monica, G. [CA/US]; 15600 Marathon Circle, Apt. 202, North Potomac, MD 20878 (US). NECKERS, Leonard, M. [US/US]; 5121 Wissioming Road, Bethesda, MD 20850 (US). SCHULTE, Theodor, W. [DE/US]; 4867 Battery Lane, Apt. 21, Bethesda, MD 20814 (US). (74) Agents: LARCHER, Carol et al.; Leydig, Voit & Mayer, Ltd., Two Prudential Plaza, Suite 4900, 180 North Stetson, Chicago, IL 60601-6780 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: METHOD OF INHIBITING A CHAPERONE PROTEIN (57) Abstract <p>The present invention provides a method of inhibiting binding of a chaperone protein with its client protein or client polypeptide. This method comprises contacting coumarin or a coumarin derivative with a chaperone protein, such that the coumarin or the coumarin derivative binds the chaperone protein, which inhibits the chaperone protein from binding its client protein or client polypeptide.</p>		



FOR THE PURPOSES OF INFORMATION ONLY

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REVISED VERSION

(19) World Intellectual Property Organization
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60/124,135 12 March 1999 (12.03.1999) US
- (71) Applicant (for all designated States except US): **THE UNITED STATES OF AMERICA, represented by THE SECRETARY DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; National Institutes of Health, Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **MARCU, Monica, G.** [CA/US]; 15600 Marathon Circle, Apt. 202, North Potomac, MD 20878 (US). **NECKERS, Leonard, M.** [US/US]; 5121 Wissioming Road, Bethesda, MD 20850 (US). **SCHULTE, Theodor, W.** [DE/US]; 4867 Battery Lane, Apt. 21, Bethesda, MD 20814 (US).
- (74) Agents: **LARCHER, Carol** et al.; Leydig, Voit & Mayer, Ltd., Two Prudential Plaza, Suite 4900, 180 North Stetson, Chicago, IL 60601-6780 (US).
- (81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
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- Published:
— With declaration under Article 17(2)(a); without classification and without abstract; title not checked by the International Searching Authority.
- (48) Date of publication of this corrected version:
11 January 2001
- (15) Information about Correction:
see PCT Gazette No. 02/2001 of 11 January 2001, Section II
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD OF INHIBITING A CHAPERONE PROTEIN

(57) Abstract:

WO 00/53169 A2

PATENT COOPERATION TREATY

PCT

DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT

(PCT Article 17(2)(a), Rules 13ter.1(c) and Rule 39)

Applicant's or agent's file reference 175961	IMPORTANT DECLARATION	Date of mailing (day/month/year) 27/10/2000
International application No. PCT/US 00/ 06482	International filing date (day/month/year) 10/03/2000	(Earliest) Priority date (day/month/year) 12/03/1999
International Patent Classification (IPC) or both national classification and IPC		
Applicant THE UNITED STATES OF AMERICA, represented by THE;		

This International Searching Authority hereby declares, according to Article 17(2)(a), that **no international search report will be established** on the international application for the reasons indicated below

1. ☐ The subject matter of the international application relates to:
 - a. ☐ scientific theories.
 - b. ☐ mathematical theories
 - c. ☐ plant varieties.
 - d. ☐ animal varieties.
 - e. ☐ essentially biological processes for the production of plants and animals, other than microbiological processes and the products of such processes.
 - f. ☐ schemes, rules or methods of doing business.
 - g. ☐ schemes, rules or methods of performing purely mental acts.
 - h. ☐ schemes, rules or methods of playing games.
 - i. ☐ methods for treatment of the human body by surgery or therapy.
 - j. ☐ methods for treatment of the animal body by surgery or therapy.
 - k. ☐ diagnostic methods practised on the human or animal body.
 - l. ☐ mere presentations of information.
 - m. ☐ computer programs for which this International Searching Authority is not equipped to search prior art.
2. ☒ The failure of the following parts of the international application to comply with prescribed requirements prevents a meaningful search from being carried out:

☒ the description
☒ the claims
☐ the drawings
3. ☐ The failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions prevents a meaningful search from being carried out:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.
4. Further comments:

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Claudia Aragone
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 203

The subject-matter of the present application defines the disease or disorder to be treated by the inhibition of the binding of a chaperone protein with its client protein or polypeptide with a coumarin. When the application is directed to a therapeutic application of a medicament and the condition to be treated is defined in functional terms, such as those in the application under consideration, the skilled person must be given instructions allowing him to recognise which conditions fall within the functional definition.

In the present case, the invention is based on the discovery that coumarin derivatives inhibit binding of a chaperone protein with its client protein or polypeptide. Accordingly, the therapeutic indication of coumarin derivatives is the treatment of any condition susceptible of being improved or prevented by inhibition of a chaperone protein with its client. It is stressed that the inhibition of "the binding of a chaperone protein with its client protein or polypeptide", cannot in itself be considered a therapeutic application. The discovery on which the invention is based needs to find a practical application in the form of defined, real treatment of any pathological condition in order to make a technical contribution to the art and be considered an invention eligible for patent protection.

However, the description cites no examples of such conditions intended to be treated according to the invention.

Therefore, due to the functional definition of the subject-matter of the present application, which embraces an undefined and unlimited number of conditions capable of being improved or prevented by the inhibition of a chaperone protein with its client, and in absence of examples in the description of such conditions intended to be treated, the present application lacks clarity (Article 6 PCT). This lack of clarity in the present case is such as to render a search impossible.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.